

But, as stated above, the experiments, though striking in their results, were rather of a domestic character than of physical precision. However this may be, the difference between ordinary and "caffeine-free" coffee affords a further proof that the toxic effect is principally due to the presence of the caffeine.

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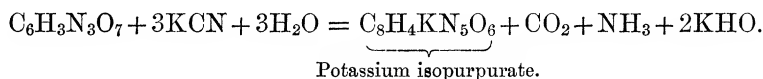
*A New Method for the Quantitative Estimation of Hydrocyanic Acid in Vegetable and Animal Tissues.*

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The evolution of hydrocyanic acid by laurel leaves (*Prunus laurocerasus*) in consequence of congelation, or of their exposure to the action of anæsthetic vapours, was first pointed out by Raphael Dubois.\* It has been studied more recently by Guignard,† who has introduced an extremely delicate test for the presence of hydrocyanic acid by sodium picrate paper, and quite recently this test has been applied by F. E. Armstrong‡ for the rapid detection of ferments of the emulsin class. The reaction was first studied by Hlasiwetz§ in 1859, who gave the following equation:—



The reaction appeared likely to afford a convenient instance for the simultaneous observation of chemical and electrical changes taking place in living protoplasm under the influence of anæsthetics, and the immediate purpose of this investigation was to determine the parallelism or the want of parallelism between the course of the two changes—chemical and electrical.

Qualitative experiments in which the evolution of hydrocyanic acid from laurel leaves was followed by means of picrate paper, the leaves being enclosed in corked tubes containing the vapour of (1) chloroform; (2) ether; (3) alcohol; and (4) water, gave results in the order of intensity (1), (2), (3),

\* R. Dubois, 'Richet's Dictionnaire de Physiologie,' art. "Hydratation."

† Guignard, 'Bulletin des Sciences Pharmacologiques,' 1906, p. 415.

‡ E. F. Armstrong, 'Physiol. Soc. Proc.,' March 19, 1910.

§ Hlasiwetz, Liebig's 'Annalen,' vol. 110, p. 289, 1859.

and (4), both as regards evolution of HCN and decline of electrical response. In chloroform vapour the evolution of HCN was greatest, and the abolition of electrical response most rapid. In water vapour there was no evolution of HCN and no diminution of electrical response, so that it appeared at first sight as if the two kinds of effect, increasing in the first case, decreasing in the second, were the associated consequence of the same disturbance of protoplasm.

But on further examination, more especially by quantitative experiments in which the degree of anæsthetic action was graduated and the evolution of hydrocyanic acid estimated, this view proved to be untenable.

In order to make *quantitative* experiments it was necessary to use the anæsthetic reagents in aqueous solution. By preliminary trials it was found possible to do so in weak solution of sodium picrate, which, in the absence of an anæsthetic, was found to have little or no toxic action upon the leaves. A leaf immersed in "picrate fluid"—0.05 per cent. picric acid + 0.5 per cent. sodium carbonate—remains alive for many days, with an undiminished electrical response and without any evidence of HCN evolution, whereas a leaf immersed in the same solution + 0.4 c.c. chloroform per 100 c.c. loses its electrical response and reddens the liquid, in a few hours at ordinary temperatures (16° to 18°), in a few minutes at a temperature of 40°. Similar results are obtained with "picrate fluid" + 5 c.c. ether per 100 c.c., or 20 c.c. ethyl alcohol per 100 c.c.

The varying tints obtained, obviously dependent upon varying amounts of hydrocyanic acid evolved, led me to make experiments with various mixtures containing known small amounts of hydrocyanic acid, in order to see whether a reliable colour scale could be obtained. Equal volumes of picrate fluid and HCN solution (titrated by  $\text{AgNO}_3$ ) at concentrations 0.1, 0.01, 0.001, and 0.0001 per cent. gave tints which on appropriate dilution were found to be reasonably concordant, and stable even when exposed to direct sunlight. It was found necessary that the picrate should be taken in great excess in relation to the cyanide, and that in any case, by reason of the slowness of the reaction, comparisons of tint should be taken 24 hours after mixture at ordinary temperatures, or after an hour or two in an incubator at 40°.

*The Colour Scale.*—The mixture adopted as standard is made from equal volumes of picrate fluid and 0.002-per-cent. HCN left for 24 hours in an incubator at 40°. This mixture contains 10 milligrammes HCN per litre, and has a red colour of an intensity T 10, where T 1 denotes the tint corresponding with 1 milligramme HCN per litre, or 1 millionth gramme per 1 c.c. The colour T 10 is nearly matched by the colour of a 5-per-cent.

solution of potassium bichromate. It is a very "fast" colour—not being appreciably affected by direct sunlight or by boiling.

Thus a tint of T 1 in 1 c.c. liquid represents 0.000001 gramme HCN.

T 1 in 15 c.c.	„	0.000015	„
T 5 in 20 c.c.	„	0.000100	„
T 10 in 100 c.c.	„	0.001000	„

For actual comparison it is preferable to dilute a given liquid, if very highly coloured, so as to bring it below the intensity T 10. For delicate estimations, as *e.g.* of HCN in the blood of an animal poisoned by inhalation of HCN, it is possible to distinguish with certainty tints below the intensity T 1 (*vide infra*, Experiments 11 and 12).

The rate of development of colour in the reaction between picric and hydrocyanic acid is illustrated by the following figure. At 20° the colour of

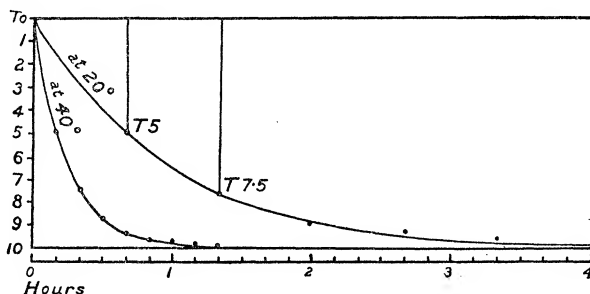


Fig. 1.—Curves showing the rate of development of colour, *i.e.* of the formation of sodium isopurpurate, in a mixture of equal volumes of picrate fluid and of 0.002 per cent. HCN, at 20° and at 40°.

a mixture of equal volumes picrate and HCN (0.002 per cent.) reached one-half its maximal value in 40 minutes, three-quarters its maximal value in 80 minutes. At 40° these times were shortened to 10 and 20 minutes respectively. From which, admitting that the time of intensification to within  $1/n$  of maximum depth of tint varies as the logarithm of  $n$ , we may calculate times of intensification to within  $1/100$  of its full depth at different temperatures. Thus the tint of a mixture should reach to within  $1/100$  of fulness, *i.e.* to  $99/100$ , in 4 hours 46 minutes at 20° and in 1 hour 6 minutes at 40°. Distillates should therefore be left in the incubator for at least an hour before their tints are estimated.

This method, by which it is easy to estimate minute quantities of HCN, counting by thousandths of a milligramme, with an error by manipulation and reading that does not, at present, amount to 10 per cent. of the reading, and that, no doubt, will be reduced by further experience, is very generally

applicable. On laurel leaves under the influence of anæsthetics, the daily or hourly evolution of HCN can be followed in a series of tubes from which the contents are decanted at stated intervals (*vide infra*, figs. 2 and 3). On animals (and on man) the tenour in HCN in blood, or in other tissues, can be quantitatively estimated by the colours of distillates from known weights of material into suitable volumes of picrate (*vide infra*, Experiments 1 to 25).

As regards its application to the particular question stated above, as to the parallelism between chemical and electrical phenomena in laurel leaves, it has furnished what, in my judgment, is a clear and unmistakable answer, to the effect that the evolution of hydrocyanic acid—so far from being a sign of life in the sense that the electrical response is a sign of life—is a sign of loss of life, and, at any rate as to its main bulk, a *post-mortem* phenomenon.

*On the Time-Relations of Electrical and Chemical Changes taking Place in Anæsthetised Laurel Leaves.*

The earliest time after exposure to  $\text{CHCl}_3$  vapour at which an evolution of HCN can be detected has, in my observation, been 5 minutes. The electrical response to a strong induction shock, *i.e.* the ingoing homodrome or antidrome blaze-current (which, as has been described at length elsewhere,\* is a characteristic sign of life), is completely abolished as early as one minute after exposure to chloroform vapour. (Young tender leaves are best adapted to this experiment. Older leaves, by reason of their high electrical resistance, are not suitable.)

We may not infer from the time-difference alone that the evolution of HCN is a *post-mortem* phenomenon, since it may be due to “lag” in the production and diffusion of HCN, and in the reaction of HCN with picric acid.

But a leaf which, after a minute’s exposure to  $\text{CHCl}_3$  vapour, has lost its electrical excitability, and which begins to give signs of HCN 10 minutes later, and goes on giving off HCN for hours and days is assuredly dead. The HCN is then, in the main, a product of *post-mortem* action in a leaf that was killed during the first minute.

The following figures will be sufficient to illustrate the course of this *post-mortem* fermentation, which, like other chemical actions, takes place more rapidly at higher than at lower temperatures:—

\* Waller, ‘Lectures on the Signs of Life,’ 1903, p. 87 (§ 55), p. 94 (§ 59), p. 109 (§ 65).

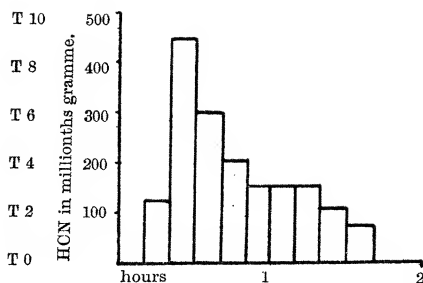


Fig. 2.—Laurel leaf weighing 2.3 grammes, in weak picrate +  $\text{CHCl}_3$  4/1000; fluid decanted every ten minutes and compared with a colour scale. Incubator at  $40^\circ$ .

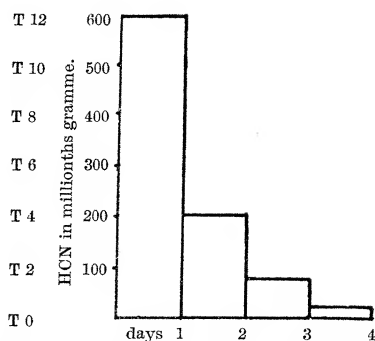


Fig. 3.—Laurel leaf weighing 2 grammes, in 50 c.c. weak picrate +  $\text{CHCl}_3$  4/1000; fluid changed each day and compared with a colour scale.

*Quantitative Estimation of Hydrocyanic Acid in the Blood and Tissues of Animals, and of Man, after Death by Hydrocyanic Acid Poisoning.*

Estimations were made by distilling the blood or minced tissue, mixed with water acidified by tartaric acid, into a solution of sodium picrate. They have been made with the blood and other tissues of animals that had received, by intravenous injection or by injection into the stomach, amounts of hydrocyanic acid, or of potassium or sodium cyanide, much above and rather below the reputed minimum lethal dose; also with the blood and tissues of animals that had died by inhalation of HCN, in whose blood therefore the actual amounts of HCN inhaled had been automatically limited by the arrest of respiration. As will be seen from the following summary of experiments, the method lends itself to the quantitative determination *post mortem* of very minute amounts of hydrocyanic acid. It is applicable up to (if not beyond) 48 hours *post mortem* (Experiment 17). And, as shown in the tabular digest giving millionths ingested per gramme of body weight and millionths found per gramme of tissue, it brings into evidence that the organs in which HCN is found to be most abundant (and for which, presumably, its affinity is relatively great) are the heart and the brain. As shown in Experiment 3, it passes in the blood itself from the plasma to the corpuscles.

The method is simple and expeditious. Each distillation requires about half-an-hour, and, as shown by fig. 1, an hour's digestion at  $40^\circ$  is sufficient to bring out the full (98 to 99 per cent.) depth of tint in the distillate.

*Experiment 1.*—Cat; weight, 2 kilos.; chloroform anæsthesia. Death by injection into the femoral vein of 10 c.c. of a 1 per cent. solution of HCN. Blood removed from the heart immediately after death and defibrinated.

10 c.c. of blood diluted with water to 75 c.c. *plus* a little tartaric acid, distilled, and the distillate received in three successive portions, each 15 c.c., in 50 c.c. of picrate of soda solution. Next day the three solutions were as follows :—

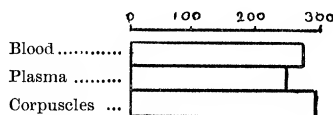
1. The first distillate (65 c.c.) had a red colour = T 8, indicating 0·000520 gramme HCN.
2. „ second „ (65 c.c.) „ „ = T 4, „ 0·000260 „ „
3. „ third „ (65 c.c.) „ „ = T 0·8, „ 0·000052 „ „

Another 10 c.c. of blood was left freely exposed to air for 48 hours and then distilled in two successive portions :—

4. The first portion was of a colour = T 1·5, indicating 0·000090 gramme HCN.
5. „ second „ „ „ = T 0·75, „ 0·000045 „ „

*Experiment 2.*—Kitten : 0·6 kilo. ; chloroform ; 10 c.c. of 1 per cent. solution of HCN poured into the stomach. Immediate death. 10 c.c. of defibrinated blood, diluted with water and distilled into 50 c.c. of sodium picrate, gave T 5 (*i.e.* 0·000300 gramme HCN).

*Experiment 3.*—Cat ; 2 kilos. ; chloroform ; 10 c.c. of 1 per cent. HCN into stomach. Immediate death. Distillation into 25 c.c. picrate.



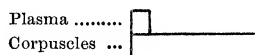
First day distillate—

- |  |                | Gramme HCN per<br>10 grammes tissue. |
|--|----------------|--------------------------------------|
| 1. From 10 c.c. of defibrinated blood diluted to 60 c.c. | T 9 in 31 c.c. | 0·000279.                            |
| 2. „ 10 c.c. of plasma .....                             | T 8 in 29 c.c. | 0·000252.                            |
| 3. „ 5 c.c. of corpuscles .....                          | T 5 in 30 c.c. | 0·000300.                            |

The difference between blood, plasma, and corpuscles as regards HCN is not very marked.

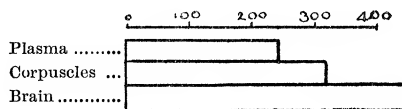
Second day distillate, the blood having been left exposed to air—

- |                              |              |           |
|------------------------------|--------------|-----------|
| 4. From 10 c.c. plasma ..... | T 0·75 × 32. | 0·000024. |
| 5. „ 5 c.c. corpuscles ..... | T 3·5 × 30.  | 0·000210. |



*Experiment 4.*—A control experiment. Cat ; 3 kilos. ; killed by chloroform. Distillates into 25 c.c. picrate from 10 c.c. of blood and from 10 grammes of brain. No change of colour in the picrate in either case.

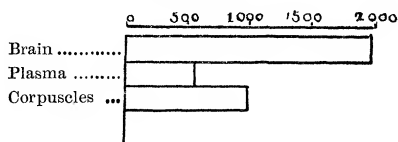
*Experiment 5.*—Cat ; 3 kilos. ; chloroform ; 10 c.c. of 1 per cent. HCN poured into the stomach ; immediate death ; distillates taken at once.



- |                                  |                       |           |
|----------------------------------|-----------------------|-----------|
| Distillate 1 from 10 c.c. plasma | gave T 7·5 in 32 c.c. | 0·000240. |
| „ 2 „ 10 c.c. corpuscles         | „ T 10 in 32 c.c.     | 0·000320. |
| „ 3 „ 10 gr. brain               | „ T 15 in 30 c.c.     | 0·000450. |

The remarkable feature here is the large amount of HCN distilled from the brain. Three days later a distillate of the second half of the brain, weighing 10 grammes, gave 0·000045.

*Experiment 6.*—Cat; 2·4 kilos.; chloroform; 10 c.c. of 1 per cent. HCN injected *per jugulam*; immediate death; brain removed at once; blood defibrinated and centrifuged at once. Materials kept in bottles till next day.



Sixteen hours later—

Distillate 1 from 10 grammes brain	gave T 60 in 33 c.c.	0·001980.
„ 2 „ 10 c.c. plasma	„ T 18 in 32 c.c.	0·000576.
„ 3 „ 10 c.c. corpuscles	„ T 30 in 33 c.c.	0·000990.

So far these are the highest numbers obtained; the exit tube from the still dipped into the picrate solution and there was no appreciable loss of HCN vapour. The colour of the brain distillate was that of port wine; the calculated amount of HCN was nearly 2 milligrammes per 10 grammes (*i.e.* 480 milligrammes per 2·4 kilos. if the poison had been equally distributed over the body of the cat; the actual injection had been 100 milligrammes or 42 milligrammes per kilo. The amount found in the brain was 198 milligrammes per kilo.).

Three days later—

Distillate 4 from 10 c.c. blood	gave T 10 in 31 c.c.	0·000310.
„ 5 „ 10 grammes brain	„ T 30 in 30 c.c.	0·000900.

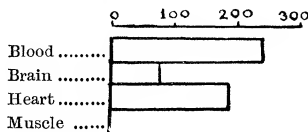
Six days later—

Distillate 6 from 10 grammes brain	gave T 10 in 30 c.c.	0·000300.
„ 6a „ 10 „ „ „	T 1 in 30 c.c.	0·000030.

*Experiment 7.*—Cat; 2·5 kilos.; chloroform; three intravenous injections of 10 c.c. 1 per cent. solution of amygdalin in the course of half-an-hour (= 100 milligrammes = 5·3 milligrammes HCN), immediately followed by 10 c.c. of 0·1 per cent. solution of emulsin. No marked effects. Finally, two injections of 10 c.c. of a freshly made mixture of equal volumes of 1 per cent. amygdalin and 1 per cent. emulsin. Death at the second injection.

The distillate into picrate of 10 c.c. of defibrinated blood gave T 1·2. 0·000072.

*Experiment 8.*—Cat; 2·4 kilos.; chloroform, 2 per cent.; 10 c.c. of 1 per cent. HCN solution (0·1 gramme) poured into stomach; immediate death. Distillates taken from 10 grammes.



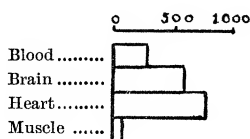
Distillate 1. Blood	.....	T 8 in 30 c.c.	0·000240.
„ 2. Hind brain	.....	T 1 in 30 c.c. × 2.	0·000060.
„ 3. Fore brain	.....	T 1·25 in 30 c.c. × 2.	0·000075.
„ 4. Heart muscle	...	T 6 in 30 c.c.	0·000180.
„ 5. Gluteal muscle	...	T 0 in 28 c.c.	Nil.

The remarkable point in this experiment was the presence of HCN in cardiac muscle, its absence from skeletal muscle. Subsequent experiments show that this difference is a characteristic feature.

*Experiment 9.*—Cat; 2·7 kilos.; chloroform, 2 per cent.; 10 c.c. of 2 per 10,000 HCN solution (0·002) injected by the femoral vein lowered the blood pressure; then 10 c.c. 1 per 1000 (0·01) killed the animal.

Distillate 1. Blood .....	T 2	in 30 c.c.	0·000060	gramme HCN.
„ 2. Brain .....	T 2	in 29 c.c.	0·000058	„ „
„ 3. Heart .....	T 3·5	in 31 c.c.	0·000108	„ „

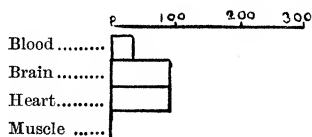
*Experiment 10.*—Cat; 3 kilos.; chloroform, 2 per cent.; 10 c.c. of 0·5 per cent. HCN solution (0·05 gramme) injected by the femoral vein. Distillates from 10 grammes.



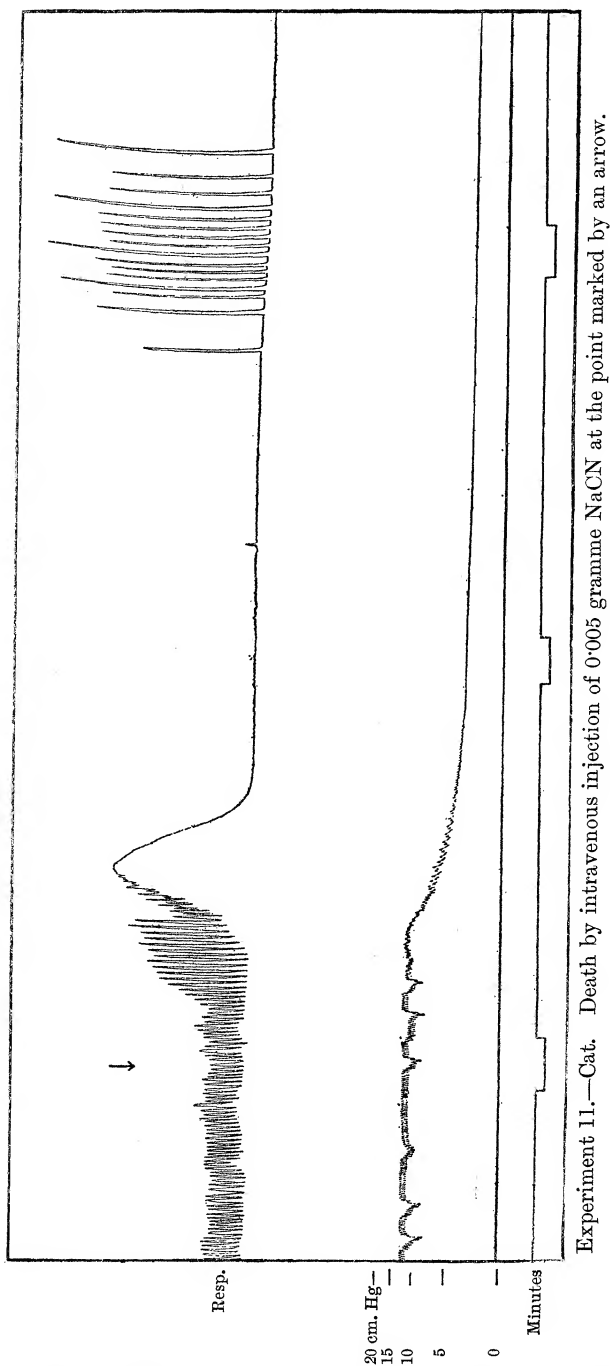
Distillate 1. Blood.....	T 7 × 30 (+T 3 × 30).	0·000300	gramme HCN.
„ 2. Brain.....	T 16 × 31 (+T 3 × 32).	0·000592	„ „
„ 3. Heart ...	T 25 × 31 c.c.	0·000775	„ „
„ 4. Muscle ...	T 3·5 × 31	0·000108	„ „

*Note.*—The heart weighed 12·3 grammes. The brain weighed 23·2 grammes.

*Experiment 11.*—Cat; 2·2 kilos.; chloroform, 2 per cent. Death by injection of 1 c.c. of 0·5 per cent. solution of NaCN (= 5 milligrammes NaCN = 2·6 milligrammes CN). Distillates of 10 grammes into 10 c.c. picrate.



Distillate 1. Blood .....	T 1·5 × 20.	0·000030	gramme HCN.
„ 2. Brain .....	T 4·5 × 20.	0·000090	„ „
„ 3. Brain (2nd distillate) ...	T 0 × 20.	Nil.	
Distillate 4. Heart .....	T 4·5 × 20.	0·000090	„ „
„ 5. Muscle.....	T 0 × 21.	Nil.	



Experiment 11.—Cat. Death by intravenous injection of 0.005 gramme NaCN at the point marked by an arrow.

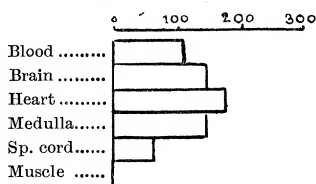
*Experiment 12.*—Cat; 2 kilos.; chloroform, 2 per cent. Death by injection of 1 c.c. of 0.5 per cent. solution of KCN (= 5 milligrammes KCN = 2 milligrammes CN). Distillates of 10 grammes into 10 c.c. picrate.

Distillate 1. Blood .....	T 2.5 × 21.	0.000052 gramme HCN.
„ 2. Brain .....	T 4.5 × 20 × 10/8.	0.000112 „ „
„ 3. Heart .....	T 2.0 × 20.	0.000040 „ „
„ 4. Muscle.....	Nil.	Nil.
„ 5. Brain (2nd distillate) ...	Nil.	Nil.

*Experiment 13* (June 9, control).—Cat ; 2.5 kilos. ;  $\text{CHCl}_3$ , 2 per cent. for 68 minutes, then at 5 per cent. for 6 minutes. Death. Distillates (20 c.c.) of 10 grammes of blood, brain, and heart into 10 c.c. picrate gave T 0, *i.e.* no HCN.

*Experiment 14* (June 9, control).—Cat ; 2.6 kilos. ; ether, 12 per cent. for 23 minutes, then raised to 20 per cent. for 13 minutes. Death by pithing. Distillates as above, of blood, brain, and heart, gave no colour change, *i.e.* no HCN.

*Experiment 15* (June 10).—Cat ; 2.8 kilos. ; ether at 20 per cent. for 13 minutes. Respiration stopped, but immediately restored by artificial means. Ether at 12 per cent. Thirty-one minutes later, death by intravenous injection of 5 c.c. of 1 per 1000 HCN (= 5 milligrammes). Distillates as usual.



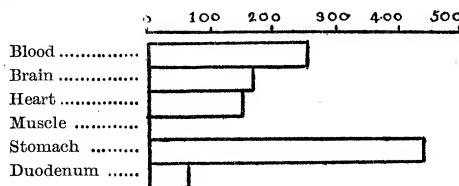
Distillate 1. Blood .....	T 5 × 22 c.c.	0.000110.
„ 2. Brain .....	T 6.5 × 22 c.c.	0.000143.
„ 3. Heart .....	T 7 × 25 c.c.	0.000175.
„ 4. Medulla .....	T 6 × 23 c.c.	0.000138.
„ 5. Spinal cord ...	T 3 × 21 c.c.	0.000063.
„ 6. Muscle.....	T 0 × 21 c.c.	Nil.

*Experiment 16*.—Cat ; 2.6 kilos. Death in one minute by inhalation of 1 per cent. HCN on blotting paper.

1. Blood .....	T 0.75 × 20 c.c.	0.000015.
2. Brain .....	T 0.5 × 20 c.c.	0.000010.
3. Heart .....	T 0.75 × 20 c.c.	0.000015.
4. Muscle .....	T 0 × 20 c.c.	Nil.

*Note*.—No estimate is possible of the amount of HCN actually inspired. Judging from the amounts found as compared with those found in the previous experiment, the amount inspired must have been much below 5 milligrammes.

*Experiment 17* (June 11).—Cat ; 2.8 kilos. ; ether. Death by 5 c.c. of 1 per cent. HCN poured into stomach. Body left untouched for 50 hours, when the usual distillates were taken, with these results :—



1. Blood .....	T 9 × 22 c.c.	2nd dist. T 3 × 19	0·000198 + 0·000057.
2. Brain .....	T 6 × 20 c.c.	„ T 2 × 22	0·000120 + 0·000044.
3. Heart .....	T 6 × 19 c.c.	„ T 1·15 × 22	0·000014 + 0·000033.
4. Stomach wall .....	T 15 × 20 c.c.	„ T 6 × 23	0·000300 + 0·000138.
5. Duodenum wall ...	T 1·5 × 21 c.c.	„ T 1·25 × 24	0·000031 + 0·000030.
6. Muscle .....	T 0 × 20 c.c.		Nil.

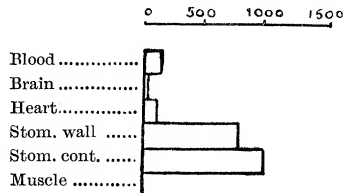
*Note.*—This experiment shows that after an excessive dose of HCN the poison is discoverable in the walls of the stomach especially, as well as in other organs and in the blood, under the ordinary conditions of a delayed *post-mortem* investigation. It also indicates, by the amounts found in 2nd distillates, that a first distillation may have failed to recover all the HCN present in the blood and tissues.

*Experiment 18.*—Cat ; 2·7 kilos. ; ether ; tracheotomy. Death in half a minute by inhalation through a Woulfe bottle over a 1 per cent. solution of HCN. Distillates as usual.

1. Blood.....	T 6 × 21 c.c.	0·000126.
2. Brain.....	T 4 × 20 c.c.	0·000080.
3. Heart .....	T 7 × 22 c.c.	0·000156.
4. Muscle .....	T 0 × 21 c.c.	Nil.

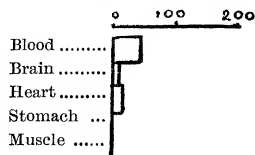
*Note.*—An approximation to the amount of HCN inhaled was arrived at as follows. The animal stopped breathing in half a minute, having inhaled 600 c.c. of air. A litre of air driven through the Woulfe bottle in one minute into 100 c.c. picrate gave T 120, viz. 0·012000, ∴ the amount inhaled was 0·007200 gramme.

*Experiment 19.*—Cat ; 3·2 kilos. ; urethane and chloroform. Death after three successive injections into the stomach of 5 c.c. 1/1000 HCN (in all 15 milligrammes). Body set aside for 24 hours. Distillates as usual.

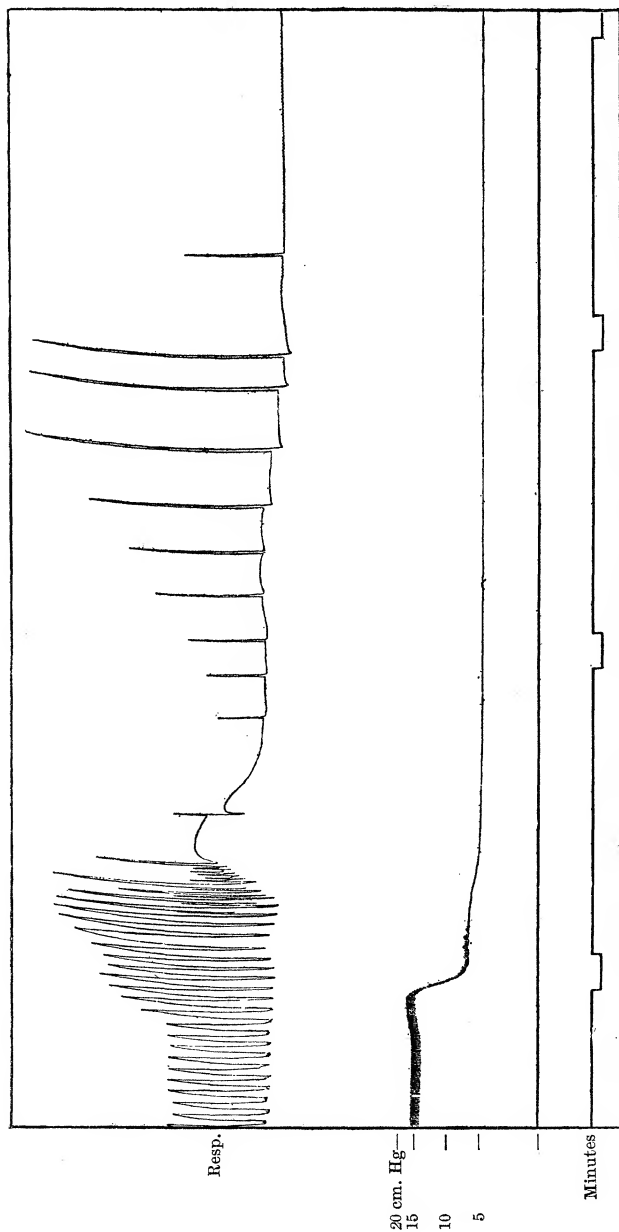


Blood (taken before administration of HCN)...	T 0 × 20	Nil.
„ (after death) .....	T 7 × 22	0·000154.
Brain .....	T 0·75 × 23	0·000017.
Heart.....	T 5 × 22	0·000110.
Stomach wall .....	T 30 × 21 + T 5 × 22	0·0006300 + 0·00011.
„ contents (consisting of 8 c.c. liquid)...	T 40 × 20 + T 6 × 21	0·000800 + 0·000126.
Muscle .....	T 0 × 20	Nil.

*Experiment 20* (June 15).—Cat ; 2·9 kilos. ; ether. Death by subcutaneous injection of 1 c.c. 1 per cent. HCN (= 10 milligrammes).



Distillates of blood.....	T 2 × 20	0·000040.
„ brain.....	T 0·5 × 20	0·000010.
„ heart.....	T 1 × 20	0·000020.
„ stomach .....	T 0 × 20	Nil.
„ muscle .....	T 0 × 20	Nil.



Experiment 18.—Cat. Death by inhalation through a Woulfe bottle containing a 1 per cent. solution of HCN. The arrow points to the commencement of inhalation. The sudden fall of blood-pressure occurs 20 seconds later.

*Experiments 21 to 25 added to paper August, 1910.*

*Experiment 21* (June 17).—Cat ; 3·2 kilos. ; ether. Death in one minute by intravenous injection of 10 milligrammes HCN. Blood drawn off before the injection and after death. Distillates as usual, taken on June 17, 18, and 20.

		grammes HCN.
June 17.—Blood (before injection) .....	T 0	0·000000.
Blood (after death) .....	T 5 × 25	0·000125.
Brain .....	T 8 × 25	0·000200.
Liver .....	T 5 × 21	0·000105.
Spleen (4 grammes) .....	T 2 × 10/4 × 21	0·000105.
Gall-bladder (3·3 grammes) .....	T 0·4 × 3 × 22	0·000026.
Muscle .....	T 0·2 × 20	0·000004.
June 18.—Blood .....	T 5 × 22	0·000110.
Brain .....	T 6 × 21	0·000126.
June 20.—Blood .....	T 2 × 20	0·000040.
Heart .....	T 5 × 20	0·000100.
Liver .....	T 1·5 × 20	0·000030.

*Experiment 22* (June 22).—Cat ; 2·5 kilos ; ether. Death in 10 minutes by inhalation over a 1/1000 solution of HCN. Distillates taken same day.

Blood .....	T 0·75 × 21	0·000016.
Brain .....	T 0·5 × 23	0·000011.
Heart .....	T 0·5 × 22	0·000011.
Muscle .....	T 0·2 × 22	0·000004.
Stomach .....	T 0·5 × 23	0·000011.
Lungs .....	T 0·5 × 22	0·000011.

*Experiment 23* (June 22).—Cat ; 2·3 kilos. ; ether. Death in 10 minutes by inhalation over 1/1000 solution of HCN. Distillates as usual.

Blood .....	T 0·75 × 21	0·000016.
Brain .....	T 2·0 × 22	0·000044.
Heart .....	T 1·5 × 23	0·000034.
Lung .....	T 0·75 × 22	0·000016.

In this as well as in the preceding experiment there was more HCN in the heart and in the brain than in the lung, although the poison had been taken in by inhalation.

*Experiment 24* (June 23).—By courtesy of Dr. Freyberger. Male, aged 60, found dead in bed on the morning of June 21. Distillates as usual.

Blood .....	T 2 × 20	0·000040.
Brain .....	T 1 × 20	0·000020.
Heart .....	T 2 × 20	0·000040.
Muscle .....	T 0·5 × 20	0·000010.
Viscera .....	T 20 × 20	0·000400.

*Experiment 25* (June 25).—A control observation, by courtesy of Dr. Freyberger. Female, aged 50. Death under chloroform. Distillates as usual. No sign of HCN in blood, brain, heart, muscle, or viscera.

HCN injected, expressed in millionths gramme per gramme body weight.		HCN found, expressed in millionths gramme per gramme tissue.				
		Blood.	Brain.	Heart.	Muscle.	
Expt.						
1. By vein .....	50	83	—	—	—	plasma 25, next day 2·5; corpuscles 30, next day 21.
2. „ stomach .....	167	30	—	—	—	
3. „ „ .....	50	28	—	—	—	
4. Control.....	0	0	0	—	—	plasma 24, corpuscles 32. „ 58, „ 99.
5. By stomach .....	30	—	45	—	—	
6. „ vein.....	42	—	198	—	—	
7. „ „ potentially in amygdalin	4	7	—	—	—	
8. By stomach .....	42	24	7	18	0	
9. „ vein.....	4·4	6	6	11	—	
10. „ „ .....	16·7	30	59	77	11	
11. „ „ as NaCN .....	1·2	3	9	9	0	
12. „ „ as KCN .....	1	5	11	4	0	
13. Control .....	0	0	0	0	—	
14. „ .....	0	0	0	0	—	
15. By vein .....	1·8	11·0	14·3	17·5	0	medulla 14, cord 6.
16. „ inhalation .....	(?)	1·5	1·0	1·5	0	
17. „ stomach .....	18	25·5	16·4	14·7	0	stomach 44, duodenum 6.
18. „ inhalation .....	(?) 3·0	12·6	8	15·6	0	
19. „ stomach .....	4·7	15·4	1·7	11	0	stomach wall 74, stomach content 92·6.
20. Subcutaneously .....	3·4	4	1	2	0	stomach 0.

This table, in which the numbers express millionths of a gramme per gramme (or milligrammes per kilogramme) injected and extracted, shows very clearly that hydrocyanic acid goes to some organs (*i.e.* to the heart and to the brain) rather than to others (*i.e.* the muscles). This is particularly evident where the quantity of poison injected has been very small, *i.e.*, in Experiments 11, 12, and 15.